MORGAN (J. D.)

THE CONSIDERATION OF UREA IN THE URINE.

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THE CONSIDERATION OF UREA IN THE URINE.*

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The disproportion, in certain diseases, between the active symptoms and the marked diminution of urea in the urine has recently occurred so frequently in the writer's practice, that he has been tempted to put together a few physiological facts, backed by clinical experience, in the hope of engendering a disputation upon the subject.

That urea should be thrown off in the proportion of three and a half grains † (Roberts) to each pound of body weight, to insure a safety approximation of nitrogenous waste, is an axiom familiar to us all; but the question often arises, how to explain and what to do when the urea continues nearer the normal standard of uric acid excretion than its own, or, as occurred in one of the cases here reported, an excretion of fifteen grains (1.00 gram) in twenty-four hours instead of one hundred and ninety (12.7 grams) with no perceptible signs of its retention, save from a fortunate examination of the urine. And, right here, it may be well to ask the question, Do urea and uric acid excreted in the urine stand in constant proportion? Haig (1) has arrived at such an estimate, plac-

* Read before The Medical and Surgical Society of the District of Columbia, March 9, 1896.

† Haig's ratio 3 to 1.

1 *Med. Record*, April 6, 1895.

ing the normal ratio as 1 of uric acid * to 33 of urea. This theory is completely overthrown by the experiments of Schultze, Hirschfeld, Busquet, and others. The excretion of uric acid in each individual is a fairly constant quantity, while that of urea has a wide range in variation.

Hester and Smith (2) give the following comparison of *urea and uric acid* of a *person in health:*

Urea 38.82
Uric acid.. 0.738 } Ratio, 1:54.

In a *neurasthenic patient:*

Urea 23.999
Uric acid... 0.637 } Ratio, 1:37.

Being acquainted with the facts, can we rest content and await the appearance of distinctive symptoms, trusting that the other proteids may regulate the natural waste? If we can always depend upon these constituents, such as uric acid, allantoin, creatinin, and the uric-acid leucomaines to make up the deficiency, we would be less disturbed, but only too often these bodies, which constitute the chief ingredients of normal urine, of the nitrogenous type or protein derivation, are *pari passu* decreased in the urine.

"The uric-acid leucomaines (3) are a group of bodies, closely related to uric acid, of which paraxanthin, xanthin, and gerontin are poisonous; and xanthin-creatinin is a poisonous leucomaine of the creatinin group. It is quite possible that all of these poisonous leucomaines may contribute to the production of complex

* Parkes' ratio 1 to 45.
2 *N. Y. Med. Jour.*, June 4, 1892.
3 B. K. Rachford, M. D., *Med. Record*, June 22, 1895.

symptoms. Paraxanthin and xanthin are poisonous leucomaines of the uric-acid group, capable of producing the most profound nervous symptoms. Paraxanthin is found in normal urine in very small quantities. A case of migraine is reported which, during and after the attack, showed an excess of uric acid, paraxanthin, and xanthin, and a diminished quantity of urea. Another case of epilepsy, where the urine passed, during and after an attack, showed a decrease in urea and a large increase in uric acid and paraxanthin. Ten days after the attack a urinalysis failed to show even a trace of paraxanthin and only a small quantity of xanthin, with the normal amount of urea."

The constituents of waste of nitrogenous origin are so intimately associated together in their formation within the body, that the feeding of an animal (dog) with one of these products, is very likely to produce in the urine an increase of an allied product, and vice versa. The administration of uric acid to dogs was found by Salkowski to increase allantoin and oxalic acid in the urine of the animal. If animals are fed on creatin, the creatinin in the urine is increased, but the large proportion of creatin in the muscles is ultimately converted into urea.

Recent experiments [4] seem to prove that uric acid and certain xanthin-bases are normal excretions of the alimentary mucous membrane. Investigations have shown that a variable quantity of these bodies are always to be found in the fæces; so that, hereafter, in a study of the excreta, the portion thrown off by the mucous membrane of the intestinal canal is to be given due consideration.

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[4] Weintrand. *Centralblatt fur Medicin innere* '95, No. 18.

These products of excrementitious nitrogenous waste are, as a rule, singularly and collectively increased or decreased by the same variety of food, or by the same class of diseases. It should be remembered, that when the diet is small, almost the whole of the nitrogen, which enters the body in the food is discharged from it in the form of urea; and also should there be a luxus [5] consumption of albuminoids beyond the tissue needs, the quantity of urea excreted is proportionally raised. Urea, in some hepatic conditions, takes to itself almost the whole of the albuminoids, and so it comes to pass that "the variations [6] in the quantity of urea excreted constitute an expression of the changes in nitrogenous metabolism, and, as such, possess definite clinical value."

Urea is even yet considered a toxic body by many. "My conclusions [7] are that urea is not a toxic substance—or rather is not toxic in the quantity found in any known pathologic state. Man can retain with impunity four times the amount of urea formed in twenty-four hours. Urea, according to Bouchard, is a diuretic. While, then, this product of disassimulation causes the kidneys to secrete, it not only makes its own escape, but likewise removes other waste material from the system. The non-excretion of urea makes a renal barrier, and so if urea is diminished other waste products are apt to be reduced; and in this way the quantity of urea becomes a criterion, to a certain extent, of the toxic matter retained within the system."

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[5] Fothergill.

[6] Purdy. *Urinary Diagnosis.*

[7] Harvey Cook, M. D., *Journal American Medical Association*, February, 1895.

The relations of degenerative changes in the liver to urea formation have recently been much elucidated by Noel Paton, who points out that two functions of the liver exist—bile formation and urea formation—and moreover that they bear a direct relationship to each other. It is a generally accepted fact that the chief seat of urea formation is in the liver; pathological evidence strongly supports this view. Uric acid, like urea, is a nitrogenous product, and corresponds with urea in its protein origin, and is formed chiefly in the liver. The synthesis of ammonium and lactic acid in birds is a precursor of uric acid, but in mammals it is the most important precursor of urea.

"We have seen in what large quantities urea can be retained within the system without infection,[8] and there is no proof that uric acid is in any way toxic to the organism, even when injected into the blood in enormous doses. Dr. Oliver estimates the amount of bile salts in normal urine as about one part in 10,000. The bile salts are toxic in almost infinitesimal doses; they are not only toxic, but in aqueous solution of two per cent. they kill one kilogramme of weight. Bouchard claims that in twenty four hours a man makes, by activity of his liver alone, enough poison to kill three men of his own weight. In cases of chronic interstitial nephritis—granular kidney—a decided and persistent decrease in the bile acids in the urine is noticed."

Case I.—Mrs. R., white, aged 36, nultipara, came under my care in the spring of 1895, for a supposed ganglion of the forearm. She had been under the care of several practitioners of note without improvement in the swell-

[8] Purdy's *Urinalysis*.

ing, and as a dernier resort, being told that she would have to be etherized and the tumor extirpated, she came to consult me, with the purpose of finding out if I could get rid of the tumor without the necessity of etherization. She attributed the swelling to a strain of the arm, while in bathing at Atlantic City the summer before. While treating the tumor, which was really a tophiacous mass, having slightly opened it and packed it with iodized silk thread a similar swelling began on the other arm. My interest was now more than aroused, and after another examination, a sample (one litre) of urine was requested. The first urinalysis showed a large decrease in the uric acid and urea excretions, the urea being but 6.00 grams (90 grains) in twenty-four hours in a person weighing one hundred and twenty-two pounds. This great deficiency in urea continued for some weeks, rising sometimes to nine, ten, and eleven grams. By a persistence in the treatment the excretion has now risen to 19.00 grams (285 grains). This case was marked by the appearance of a large number and variety of cells and casts from the kidneys, extending over a period of nearly a year. Albumin was abundant at times, and on several visits an œdema of the ankles was to be noticed. These casts have now all disappeared, but at times a few epithelia and granular cells are to be found, with always traces of albumin. The patient's general condition is now excellent, and is apparently perfectly well. It might be added that these tophi, which had appeared in a few other regions of the body other than the forearms, needed no further treatment than attention to the kidneys.

Case II.—Miss B., white, aged 14. Had scarlet-fever when four years of age. Always enjoyed good health, except for the past two years "would break out with hives on eating some particular article of food." She had been under treatment, but urine was never examined. First analysis showed the astonishing fact of but 1.00 gram of urea in two litres of urine. The uric acid was diminished, and there was no albumin present. The quantitative test for urea was made several times to verify the analysis, and a little over a litre of urine was at hand for examination. This patient was sitting in the parlor upon my first visit, suffering apparently from nothing but a recurrence of "hives." Three days afterwards the urine was again examined, and showed 15.00 grams of urea (225 grains), with no albumin, but oxalate of calcium crystals and granular casts. When the urea and uric acid are excreted freely, the patient suffers little with "hives," but she requires close attention to ward off relapses.

CHEMICAL LABORATORY, MEDICAL DEPARTMENT,
UNIVERSITY OF GEORGETOWN,
WASHINGTON, D. C., August 14, 1895.

Analysis for Dr. J. D. Morgan.—Name of patient, Miss B. Amount of urine in 24 hours, ——. Reaction, neutral. Color, pale. Specific gravity, 1003. Odor, odorless. Sediment, slight.

Normal Constituents.—Urophæine, —; urea, —; chlorides, N; earthy phosphates, —; indoxyl, —; uric, —; sulphates, —; alkaline phosphates, —.

Abnormal Constituents.—Albumin, —; bile pigment, —; sugar, —.

Quantitative.—*Urea, 1 grm.* per litre. Phosphoric acid, .84 grms. per litre. Chlorides, 6.5 grms. per litre. Solids by sp. gravity, 7 grms. per litre. Albumin, 0 per cent. Sugar, 0 per cent.

Microscopical.—Bladder epithelium, and very few amorphous urates.

Remarks.—Notice very small amount of *urea* excreted.

F. D. LEE, *Analyst.*

WASHINGTON, D. C., Aug. 17, 1895.

Analysis for Dr. J. D. Morgan.—Name of patient, Miss B. Amount in 24 hours, ——. Reaction, slightly alkaline. Color, straw. Specific gravity, 1012. Odor, urinous. Sediment, slight.

Normal Constituents.—Urophæine N.; urea, N.; chlorides N; earthy phosphates, —; indoxyl, N.; uric acid, —; sulphates + alkaline phosphates, N.

Abnormal Constituents.—Albumin, 0.; bile pigment, 0.; sugar, o.

Quantitative.—Urea, 15 grms. per litre. Phosphoric acid, 1.5 grms. per lit e. Chlorides, 8 grms. per litre. Solids by sp. gravity, 28 grms. per litre. Albumin, 0 per cent. Sugar, 0 per cent.

Microscopical.—Oxalate calcium, bladder cells, granular casts (few), amorphous urates.

F. D. LEE, *Analyst.*

CASE III.—Mr. McC., white, aged 60. Enjoyed good health except his autumnal attacks of hay fever, which have occurred with chronological exactness for the past ten years. A recurring wakefulness in the early morning hours caused him to send for me. After various seemingly indicated remedies failing, a quantity of his urine was examined, and the following letter will explain the result of the urinalysis:

ARMY MEDICAL MUSEUM LABORATORY,
November 14, 1895.

My Dear Doctor:

The density of the urine is low—1007 at 60° F.—and the urea amounts to but 3½ grains per ounce, so that if Mr. McC. voided 50 ounces of urine in twenty-four hours it would contain only 175 grains against considerably over 400 which it should contain.

There is also a faint trace of albumin in it, so that it looks rather serious.

Faithfully yours,
W. M. MEW.

Recently he has been suffering with very pronounced symptoms of cirrhotic kidney, but the retention of urea has evidently been going on for months, with no marked symptoms of its deficiency.

CASE IV.—One of the young busy practitioners of our city, who delights in examining a variety of urines, one day thought he would examine his own, especially as he had recently been suffering daily with headaches. You may imagine his surprise and depression when he found the urea diminished about 16.00 grams, with abundance of hyaline and granular casts, and some epithelear and fatty. Not satisfied naturally with his own examination, he sought another urinologist of our city, only to find a confirmation of the first analysis.

It has come to be regarded that casts and traces of albumin alone within the urine are not the chief pathognomonic signs on which we may give a prognosis, nor is the deficiency of urea the *bête noir* of a urinologist. Only by a grouping of all the constituents, normal and abnormal, of the urine and the objective symptoms of the patient, can we give a trustworthy opinion, which is generally problematic, with hopes, even in the worst of cases, of a partial recovery.

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